Amendments to the Claims

Please amend the claims of the application as set forth in the claim listing below, which replaces all previous listings and versions of the claims.

1. (Currently Amended) A microbubble composition for binding to a target, comprising:

gas-filled microbubbles in a liquid carrier;

~~said microbubbles substantially having crenated~~ wherein at least 20% of said microbubbles in the liquid carrier are nonspherical microbubbles having microbubble membranes with exterior surfaces comprising outwardly-projecting wrinkles formed of excess membrane material;

wherein said nonspherical microbubbles exhibit increased deformability under shear relative to corresponding spherical microbubbles;

wherein said gas is substantially insoluble in blood; and

wherein said membranes ~~including~~ include binding targeting molecules that bind to the target.

2. (Original) The microbubble composition of claim 1, wherein the microbubble membranes comprise a lipid, protein, polymer or other surfactant, or a combination thereof.

3. (Currently Amended) The microbubble composition of claim 1, wherein greater than 50% of said microbubbles in the liquid carrier are said nonspherical microbubbles~~the gas is substantially insoluble in blood~~.

4. (Original) The microbubble composition of claim 3, wherein the gas is a fluorine-containing gas.

5. (Original) The microbubble composition of claim 1, wherein the microbubbles have a mean diameter of about 1 to about 10 micrometers.

6. (Original) The microbubble composition of claim 1, wherein the target is a receptor, and wherein the binding targeting molecules bind to the receptor.

7. (Original) The microbubble composition of claim 6, wherein the receptor is selected from the group consisting of extracellular matrix proteins, adhesion molecules, G-protein coupled receptors, cell surface proteins, cytokines, glycoproteins, peptides, lipids, glycolipids, carbohydrates or combinations thereof.

8. (Original) The microbubble composition of claim 1, wherein the targeting molecules are selected from the group consisting of peptides, peptide mimetics, aptamers, proteins, antibodies and antibody fragments, oligosaccharides, and small organic molecules.

9. (Currently Amended) A microbubble composition useful for binding to a target, comprising:

a suspension of gas-filled microbubbles in a liquid carrier, wherein at least 20% of said microbubbles ~~substantially having~~ are nonspherical microbubbles having microbubble membranes ~~having surface projections~~ with exterior surfaces comprising outwardly-projecting wrinkles formed of excess membrane material, wherein said nonspherical microbubbles exhibit increased deformability under shear relative to corresponding spherical microbubbles, and wherein said membranes further ~~including~~ include binding targeting molecules that bind to the target.

10. (Currently Amended) The microbubble composition according to claim 9, wherein said gas is a fluorine-containing gas~~surface projections comprise membrane folds~~.

11. (Original) The microbubble composition of claim 9, wherein the membranes comprise a lipid, protein or surfactant, and wherein the microbubbles have a mean diameter of about 1 to about 10 micrometers.

12. (Currently Amended) The microbubble composition of claim 9, wherein greater than 50% of said gas-filled microbubbles are said nonspherical microbubbles~~the gas is substantially insoluble in blood~~.

13. (Original) The microbubble composition of claim 12, wherein the target is a cell membrane bound receptor, and wherein the targeting molecules bind to the receptor.

14. (Original) The microbubble composition of claim 9, wherein the targeting molecules are selected from the group consisting of peptides, peptide mimetics, aptamers, proteins, antibodies and antibody fragments, oligosaccharides, and small organic molecules.

15. (Original) The microbubble composition of claim 13, wherein the receptor is selected from the group consisting of extracellular matrix proteins, adhesion molecules, G-protein coupled receptors, cell surface proteins, cytokines, glycoproteins, peptides, lipids, glycolipids, carbohydrates or combinations thereof.

16. (Currently Amended) A microbubble composition useful for binding to a target, comprising:

a suspension of microbubbles in a liquid carrier, ~~said~~ wherein at least 20% of the microbubbles ~~predominantly having~~ in the liquid carrier have non-spherical microbubble membranes with exterior surfaces comprising outwardly-projecting wrinkles formed of excess membrane material, said non-spherical microbubble membranes exhibiting increased deformability under shear relative to

corresponding spherical microbubble membranes, and said microbubble membranes comprising a binding targeting molecule for binding to the target; and

wherein the microbubbles contain a gas that is substantially insoluble in blood.

17. (Original) The microbubble composition of claim 16, wherein the membranes comprise a lipid, protein, polymer or other surfactant, or a combination thereof.

18. (Currently Amended) The microbubble composition of claim 16, wherein said gas is a fluorine-containing gas~~substantially insoluble in blood~~.

19. (Original) The microbubble composition of claim 16, wherein the microbubbles have a mean diameter of about 1 to about 10 micrometers.

20. (Previously Presented) The microbubble composition of claim 16, wherein the target is a cell membrane bound receptor, and wherein the targeting molecules bind to the receptor.

21. (Withdrawn) A method for binding microbubbles to a target, comprising:

contacting the target with a microbubble composition according to claim 1.

22. (Withdrawn) A method according to claim 21, wherein microbubble membranes of the microbubble composition include a targeting molecule attached by a spacer arm.

23. (Withdrawn – Currently Amended) A method for preparing a targeted microbubble composition, comprising:

forming gas-filled microbubbles having spherical microbubble membranes suspended in a liquid carrier;

converting at least 20% of the spherical microbubble membranes to non-spherical microbubble membranes having exterior surfaces comprising outwardly-projecting wrinkles formed of excess membrane material, wherein the nonspherical microbubble membranes exhibit increased deformability under shear relative to the spherical microbubble membranes; and

attaching to or incorporating into said microbubble membranes targeting molecules for binding to a target.

24. (Withdrawn) The method of claim 23, wherein said targeting molecules are attached to or incorporated into the membranes prior to said converting.

25. (Withdrawn) The method of claim 23, wherein said targeting molecules are attached to or incorporated into the membranes after said converting.

26. (Withdrawn) The method of claim 23, wherein said converting includes causing a partial release of gas from within the spherical microbubble membranes.

27. (Withdrawn) The method of claim 26, wherein said converting includes subjecting the spherical microbubble membranes to pressure.

28. (Withdrawn) The method of claim 27, wherein said pressure is applied by hydrostatic pressure, ultrasonic waves, or an osmotic pressure gradient across the microbubble membrane.

29. (Withdrawn) The method of claim 23, wherein the targeting molecules are selected from the group consisting of peptides, peptide mimetics, aptamers, proteins, antibodies and antibody fragments, oligosaccharides, and small organic molecules.

30. (Previously Presented) A pharmaceutical composition, comprising a microbubble composition according to claim 1, wherein the liquid carrier is a pharmaceutically acceptable liquid carrier.

31. (Withdrawn) A pharmaceutical composition according to claim 30, which is a therapeutic composition.

32. (Currently Amended) A pharmaceutical composition according to claim 30, which is a diagnostic composition.

33. (Currently Amended) A pharmaceutical composition according to claim 32, ~~which is an~~ wherein said microbubbles are effective as an ultrasound contrast agent.

34. (Withdrawn) A method for ultrasound imaging in a patient, comprising:

introducing into the patient an ultrasound contrast agent according to claim 33; and

developing an ultrasound image based upon said composition.

35. (Withdrawn) A method for therapeutic treatment of a patient, comprising administering to the patient a therapeutic composition according to claim 31.